Guidance for Industry

Recommendations for Implementing a Collection Program for Source Plasma Containing Disease-Associated and Other Immunoglobulin (IgG) Antibodies

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Submit comments on this draft guidance by the date provided in the *Federal Register* notice announcing the availability of the draft guidance. Submit comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. You should identify all comments with the docket number listed in the notice of availability that publishes in the *Federal Register.*

Additional copies of this draft guidance are available from the Office of Communication, Training and Manufacturers Assistance (HFM-40), 1401 Rockville Pike, Rockville, MD 20852-1448, or by calling 1-800-835-4709 or 301-827-1800, or from the Internet at http://www.fda.gov/cber/guidelines.htm.

For questions on the content of this guidance, contact Sharyn Orton, PhD, Center for Biologics Evaluation and Research, Office of Blood Research and Review, Division of Blood Applications, at 301-827-3524.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Biologics Evaluation and Research
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Guidance for Industry

Recommendations for Implementing a Collection Program for Source Plasma Containing Disease-Associated and Certain Other Immunoglobulin G (IgG) Antibodies

Paperwork Reduction Act

This guidance contains information collection provisions that are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501-3520). The collection(s) of information under 21 CFR 601.12(d) and (f)(2) were approved under OMB control number 0910-0338.

Contains Nonbinding Recommendations

Draft – Not for Implementation

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This draft guidance, when finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the appropriate FDA staff. If you cannot identify the appropriate FDA staff, call the appropriate number listed on the title page of this guidance.

I. INTRODUCTION

Source Plasma manufacturers might want to implement a collection program to collect Source Plasma from donors who have detectable levels of disease-associated Immunoglobulin G (IgG) antibodies and other existing IgG antibodies (see section IV). Such disease-associated IgG antibodies are antibodies that have occurred in response to exposure to disease agent or other antigens. This guidance is intended to assist you, a Source Plasma manufacturer, in submitting the appropriate information to FDA when implementing an IgG antibody collection program or when adding a new IgG antibody collection to your existing program. When finalized, this guidance will replace the draft Reviewers' Guide, "Disease Associated Antibody Collection Program," issued October 1, 1995.

FDA's guidance documents, in general, do not establish legally enforceable responsibilities. Instead, guidances describe FDA's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in FDA's guidances means that something is suggested or recommended, but not required. Insofar as this guidance adjusts reporting categories for manufacturing changes pursuant to section 506A of the Federal Food, Drug, and Cosmetic Act and 21 Code of Federal Regulations (CFR) 601.12, it does have binding effect. If you have any questions about the effect of any portion of this guidance, contact Sharyn Orton, PhD, Center for Biologics Evaluation and Research, Office of Blood Research and Review, Division of Blood Applications, at 301-827-3524.

II. DISCUSSION

Source Plasma donors participating in a disease-associated IgG antibody collection program must meet all donor suitability requirements under § 640.63 (21 CFR 640.63). Donors who have disease-associated IgG antibodies are individuals who are in good health at the time of donation and either have recovered from their illness or were exposed to the disease agent but remained asymptomatic. Donors participating in a disease-associated IgG antibody collection program possess specific IgG antibodies as a result of their exposure to the disease agent.

Source Plasma collected from donors participating in disease-associated IgG antibody collection programs and in other IgG antibody collection programs (see section IV) may be used in the manufacture of injectable products and for noninjectable products, such as controls for *in vitro* diagnostic assays.

This guidance does not include recommendations for the implementation of Immunoglobulin M (IgM) antibody collection programs; nor does it include recommendations for donors who do not meet all donor suitability requirements under § 640.63. The review and approval of collection programs for plasma containing IgM antibodies and for plasma from donors who do not meet all donor suitability requirements under § 640.63 will continue through the submission of a prior approval supplement to the biologics license application (BLA) for Source Plasma.

III. RECOMMENDATIONS

Donors of Source Plasma, including Source Plasma collected under a disease associated IgG antibody collection program, must meet donor suitability requirements under § 640.63.

We, FDA, believe that, for establishments licensed to collect Source Plasma, the implementation or expansion, consistent with the recommendations in this section, of a program involving collection from eligible donors of Source Plasma containing the following disease-associated IgG antibodies, represents a change in the product that has a minimal potential to have an adverse effect on the identity, strength, quality, purity, or potency of the product as it relates to the safety or effectiveness of the product:

1. C-Reactive Protein
2. Mononucleosis (Epstein Barr)
3. Cytomegalovirus (CMV)
4. Herpes Type I
5. Herpes Type II
6. Varicella Zoster
7. Coccidioidomycosis
8. Histoplasmosis
9. Pseudomonas
10. Rubella
11. Mumps

12. Hepatitis A (Anti-HAV)
13. Hepatitis B surface (Anti-HBs)
14. Hepatitis B core (Anti-HBc)*

    *Anti-HBc collections are included in this category because the plasma is likely to contain anti-HBs, the antibody capable of neutralizing undetectable quantities of Hepatitis B virus in the Source Plasma pools.
15. Toxoplasmosis
16. Rubeola
17. Respiratory Syncytial Virus (RSV)
18. Chlamydia
19. Hemophilus influenza
20. Parvovirus B19

Upon implementing or expanding such a program at your establishment, you must document this change in an annual report to the approved BLA and submit the report to FDA under § 601.12(d) (21 CFR 601.12(d)). Your annual report notification should confirm that donors meet all required donor suitability criteria for Source Plasma under § 640.63, and that the plasma is collected from donors who have been exposed to the disease agent but are in good health at the time of collection.

Changes to the labeling to describe the products must be submitted as a "Supplement – Changes Being Effected" (21 CFR 601.12(f)(2)(i)(E)).

IV. OTHER NATURALLY OCCURRING OR PRE-EXISTING IgG ANTIBODIES

For establishments licensed to collect Source Plasma, the implementation or expansion of a program involving collection of other naturally occurring IgG antibodies from donors meeting all donor suitability requirements under § 640.63, represents a change in the product that has a minimal potential to have an adverse effect on the identity, strength, quality, purity, or potency of the product as it relates to the safety or effectiveness of the product. As described in Section III, report the manufacturing change in an annual report (21 CFR 601.12(d)) and changes to the labeling as a "Supplement – Changes Being Effected" (21 CFR 601.12(f)(2)(i)(E)).

In addition, for collections of pre-existing red blood cell antibodies, FDA recommends that donors not currently be in an immunization program and not have been immunized, either deliberately or by transfusion, within the past twelve months. Your annual report should describe the procedures you have implemented to address this issue.

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V. EXCEPTIONS

For the collections described below, Source Plasma containing IgG antibodies may only be collected and shipped following FDA's review and approval of BLAs for the product. If the collection represents a manufacturing change to an existing BLA, FDA believes that, because of the substantial potential for adverse effect of the change on the identity, strength, quality, purity, or potency of the product, implementation of the following collections must be reported as a major change in a prior approval supplement (21 CFR 601.12(b)). In some circumstances, such collections may be made only if FDA grants a variance under 21 CFR 640.120 to permit the collections. This paragraph applies to the following collections:

- Plasma collected from donors tested and found to be positive for evidence of infection due to communicable diseases as required under 21 CFR 610.40.
- Plasma collected as a by-product of therapeutic procedures;
- Plasma collected from donors participating in an immunization program (e.g., smallpox, anthrax); and
- Plasma collected from donors who do not meet all required donor suitability criteria for Source Plasma under § 640.63.